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55 ANSWERS

133.71

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FILE COVERS 1967 - 7 Feb 2001 VOL 134 ISS 7 FILE LAST UPDATED: 6 Feb 2001 (20010206/ED)

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=> s 13 full

L443 L3

=> s 14 and hypoxia

25173 HYPOXIA

L524 L4 AND HYPOXIA

=> s 15 and PET

35377 PET

1.6 3 L5 AND PET

=> d 16 1-3 ibib abs hitstr

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2000:135450 CAPLUS

DOCUMENT NUMBER:

133:55383

TITLE:

Noninvasive detection of tumor hypoxia using

the 2-nitroimidazole [18F]EF1

AUTHOR(S):

Evans, Sydney M.; Kachur, Alexander V.; Shiue, Chyng-Yann; Hustinx, Roland; Jenkins, W. Timothy; Shive, Grace G.; Karp, Joel S.; Alavi, Abass; Lord, Edith M.; Dolbier, William R., Jr.; Koch, Cameron J.

CORPORATE SOURCE:

Schools of Medicine and Veterinary Medicine,

University of Pennsylvania, Philadelphia, PA, USA

J. Nucl. Med. (2000), 41(2), 327-336

CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER:

SOURCE:

Society of Nuclear Medicine, Inc.

DOCUMENT TYPE:

Journal

LANGUAGE: English

The noninvasive assessment of tumor hypoxia in vivo is under active investigation because hypoxia has been shown to be an important prognostic factor for therapy resistance. Various nuclear medicine imaging modalities are being used, including PET imaging of 18F-contg. compds. In this study, we report the development of

18F-labeled EF1 for noninvasive imaging of hypoxia. EF1 is a 3-monofluoro analog of the well-characterized hypoxia marker EF5,

2(2-nitro-1H-imidazol-1-yl)-N-(2,2,3,3,3-pentafluoropropyl)acetamide, which has been used to detect hypoxia in tumor and nontumor systems using immunohistochem. methods. We have studied 2 rat tumor types: the hypoxic Morris 7777 (Q7) hepatoma and the oxic 9LF glioma tumor, each grown in s.c. sites. PET studies were performed using a pharmacol. dose of nonradioactive carrier in addn. to [18F]EF1 to optimize and assess drug biodistribution. After PET imaging of the tumor-bearing rats, tissues were obtained for .gamma.-counting of the 18F in various tissues and immunohistochem. detection of intracellular drug adducts in tumors. In one pair of tumors, Eppendorf needle electrode

studies were performed. [18F]EF1 was excreted dominantly through the urinary tract. The tumor-to-muscle (T/M) ratio of [18F]EF1 in the Q7 tumors was 2.7 and 2.4 based on PET studies and 2.1, 2.5, and 3.0 based on .gamma.-counting of the tissues (n = 3). In contrast, the T/M ratio of [18F]EF1 in the 9LF glioma tumor was 0.8 and 0.5 based on PET studies and 1.0, 1.2, and 1.4 based on .gamma.-counting of the tissues (n = 3). Immunohistochem. anal. of drug adducts for the two tumor

types agreed with the radioactivity anal. In the Q7 tumor, substantial heterogeneous binding was obsd. throughout the tumor, whereas in the 9LF tumor minimal binding was found. [18F]EF1 is an excellent radiotracer

noninvasive imaging of tumor hypoxia.

IT 252736-29-1

for

RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(detection of tumor hypoxia using 2-nitroimidazole [18F]EF1)

RN 252736-29-1 CAPLUS

1H-Imidazole-1-acetamide, N-[3-(fluoro-18F)propyl]-2-nitro- (9CI) (CA CN INDEX NAME)

REFERENCE COUNT:

REFERENCE(S):

- (1) Aboagye, E; Anticancer Drug Des 1996, V11, P231 CAPLUS
- (3) Ballinger, J; J Nucl Med 1996, V37, P1023 CAPLUS
- (4) Bialik, S; J Clin Invest 1997, V100, P1363 CAPLUS
- (7) Brown, J; Int J Radiat Oncol Biol Phys 1981, V7, P695 CAPLUS
- (9) Cherif, A; J Drug Target 1996, V4, P31 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1998:622782 CAPLUS

DOCUMENT NUMBER:

129:341244

TITLE:

Preclinical development and current status of the

fluorinated 2-nitroimidazole hypoxia probe

N-(2-hydroxy-3,3,3-trifluoropropyl)-2-(2-nitro-1imidazolyl) acetamide (SR 4554, CRC 94/17): a

non-invasive diagnostic probe for the measurement of

tumor hypoxia by magnetic resonance

spectroscopy and imaging, and by positron emission

tomography

AUTHOR (S):

Aboagye, Eric O.; Kelson, Andrew B.; Tracy, Michael;

Workman, Paul

CORPORATE SOURCE:

Dep. Radiol.-MR Res., The Johns Hopkins University

School of Medicine, Baltimore, MD, 21205, USA

Anti-Cancer Drug Des. (1998), 13(6), 703-730

CODEN: ACDDEA; ISSN: 0266-9536

PUBLISHER:

SOURCE:

Oxford University Press Journal; General Review

DOCUMENT TYPE: LANGUAGE:

English A review with many refs. Hypoxia occurs to a variable extent in a vast majority of rodent and human solid tumors. It results from an inadequate and disorganized tumor vasculature, and hence an impaired oxygen delivery. A probe for the non-invasive detection of tumor hypoxia could find important utility in the selection of patients for therapy, with bioreductive agents, anti-angiogenic/anti-vascular therapies and hypoxia-targeted gene therapy. In addn., tumor hypoxia has been shown to predict for treatment outcome following radio- or chemotherapy in human cancers, the underlying mechanism for which may involve hypoxia driving genetic instability and

resulting tumor progression. Beyond oncol., utility can also be envisaged

in stroke, ischemic heart disease, peripheral vascular disease, arthritis and other disorders. Design, validation, preclin. development and

status of a fluorinated 2-nitroimidazole, N-(2-hydroxy-3,3,3trifluoropropyl)-2-(2-nitro-1-imidazolyl) acetamide (SR 4554, CRC 94/17), which has been rationally designed for the measurement of tumor hypoxia by magnetic resonance spectroscopy (MRS) and imaging (MRI), are reviewed. Application in positron emission tomog. (PET ) detection is also proposed. Design goals were: (i) a nitro group with appropriate redox potential for selective redn. and binding in hypoxic tumor cells; (ii) hydrophilic/hydrogen bonding character in the side chain

to limit nervous tissue penetration and prevent neurotoxicity; and (iii) three equiv. fluorine atoms to enhance MRS/MRI detection, located in a metabolically stable position. Redn. of SR 4554 by mouse liver microsomes

was dependent on oxygen content, with a half-maximal inhibition at 0.48 .+-. 0.06%. SR 4554 underwent nitroredn. by hypoxic but not oxic tumor cells in vitro and electron energy loss spectroscopic anal. showed selective retention in the hypoxic regions of multicellular tumor spheroids. Pharmacokinetic design goals were met. In particular, low brain tissue concns. were seen in contrast to excellent tumor levels, as measured by high performance liq. chromatog. The extent of this restricted entry to brain tumor was surprising given the overall octanol/water partition coeff. and was attributed to the hydrophilic/ hydrogen bonding character of the side chain. Quant. MRS was used to assess the retention of 19F signal in murine tumors and human tumor xenografts. The 19F retention index (FRI; ratio of 19F signal levels at

h relative to that at 45 min) ranged from 0.5 to 1.0 and 0.2 to 0.9 for murine tumors and human xenografts resp. The correlation between SR 4554retention and pO2 was not a linear one, but when FRI was >0.5, the % pO2 .ltoreq. 5 mmHg was always >60%, indicating that high FRI was assocd.

with

6

low levels of oxygenation. Finally, whole body 19F-MRI in mice demonstrated that SR 4554 and related metabolites localized mainly in tumor, liver and bladder regions. A selective MRS signal was readily detectable in tumors at doses at least 7-fold lower than those likely to cause toxicity in mice. We conclude that proof of principle is established for the use of SR 4554 as a non-invasive MRS/MRI probe for

the

detection of tumor hypoxia. Based on these promising studies, SR 4554 has been selected for clin. development.

IT167648-73-9P, SR 4554

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

RN 167648-73-9 CAPLUS

1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)-CN (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} N & \text{NO}_2 \\ N & O & \text{OH} \\ || & | \\ \text{CH}_2\text{--} \text{C--} \text{NH--} \text{CH}_2\text{--} \text{CH--} \text{CF}_3 \end{array}$$

1.6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1996:494670 CAPLUS

DOCUMENT NUMBER:

125:162343

TITLE:

Detection of hypoxia with reagents

containing 2-nitroimidazole compounds and methods of

making such reagents

INVENTOR (S):

Koch, Cameron J.; Lord, Edith M.

PATENT ASSIGNEE(S):

The Trustees of the Univ. of Pennsylvania, USA; The

University of Rochester

SOURCE:

U.S., 29 pp. Cont.-in-part of U.S. Ser. No.

978, 918, abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5540908	A	19960730	US 1994-286065	19940804
CA 2149770	AA	19940526	CA 1993-2149770	19931118
US 5843404	A	19981201	US 1996-598752	19960208
PRIORITY APPLN. INFO.:	:		US 1992-978918	19921119
			US 1994-286065	19940804

OTHER SOURCE(S): MARPAT 125:162343

AB Novel nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compd. and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., protein conjugates of the compds., reductive byproducts of the compds., and adducts formed between the compds. and mammalian hypoxic cell tissue proteins. The invention is further directed

to methods for detecting tissue **hypoxia** using immunohistol. techniques, noninvasive nuclear medicine methods (**PET**, SPECT), or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

IT 180208-73-5P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(hypoxia detection with 2-nitroimidazole compds. and

(nypoxia detection with 2-nitrolmidazole compds. an immunogenic conjugates)

RN 180208-73-5 CAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)

## IT 152721-37-4P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

RN 152721-37-4 CAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

=> s 15 and protein?

1368354 PROTEIN?

L7 4 L5 AND PROTEIN?

=> d 17 1-4 ibib abs hitstr

ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1997:752599 CAPLUS DOCUMENT NUMBER: 128:70367 TITLE: Bioreductive metabolism of the novel fluorinated 2-nitroimidazole hypoxia probe N-(2-hydroxy-3,3,3-trifluoropropyl)-2-(2nitroimidazolyl) acetamide (SR-4554) AUTHOR (S): Aboagye, Eric O.; Lewis, Alexander D.; Tracy, Michael; Workman, Paul CORPORATE SOURCE: CRC DEPARTMENT OF MEDICAL ONCOLOGY, CLINICAL PHARMACOLOGY AND NEW DRUG DEVELOPMENT TEAM, UNIVERSITY OF GLASGOW, GLASGOW, G61 1BD, UK SOURCE: Biochem. Pharmacol. (1997), 54(11), 1217-1224 CODEN: BCPCA6; ISSN: 0006-2952 PUBLISHER: Elsevier Science Inc. DOCUMENT TYPE: Journal LANGUAGE: English The aim of this work was to study the metabolic characteristics of the novel fluorinated 2-nitroimidazole hypoxia probe N-(2-hydroxy-3,3,3-trifluoropropy1)-2-(2-nitroimidazoly1) acetamide (SR-4554). HPLC and 19F NMR methods were employed to evaluate the rate of reductive metab. of SR-4554 and the nature of the resulting metabolites, resp. SR-4554 was enzymically reduced by mouse liver microsomes (1.1 0.1 nmol of SR-4554 reduced/min/mg **protein**), purified rat and human NADPH: cytochrome P 450 reductase (17.8 .+-. 0.4 and 5.0 .+-. 0.5 nmol of SR-4554 reduced/min/mg **protein**, resp.), and SCCVII tumor homogenates (2.3 .+-. 0.3 nmol of SR-4554 reduced/min/g tumor) under nitrogen. NADPH:cytochrome P 450 reductase was a major microsomal enzyme involved in the bioredn. of SR-4554 by liver microsomes. In a panel of murine and human tumor xenografts, cytochrome P 450 reductase activities were found to be low and only varied by 3-fold between different tumor types, suggesting that enzyme activities within the tumors are unlikely t.o influence markedly in vivo reductive metab. Redn. of SR-4554 by mouse liver microsomes showed a characteristic oxygen dependence with a half-maximal inhibition of 0.48 .+-. 0.06%. Thus, the reductive metab. of SR-4554 can be employed to detect the low oxygen tensions that occur within both murine and human tumors. Sol., low mol. wt. reductive metabolites of SR-4554 were identified by 19F NMR. These metabolite peaks appeared (up to 0.12 ppm) downfield of the parent drug peak. In conclusion, SR-4554 undergoes an oxygen-dependent metab. that involves NADPH:cytochrome P 450 reductase. 19F NMR is capable of identifying

167648-73-9 CAPLUS CN (9CI) (CA INDEX NAME)

**167648-73-9**, SR-4554

IΤ

RN

1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)-

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

reduced metabolites that are undetectable by HPLC.

(bioreductive metab. of hypoxia probe SR-4554)

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS L7

ACCESSION NUMBER: DOCUMENT NUMBER:

1996:494670 CAPLUS

125:162343

TITLE:

Detection of hypoxia with reagents

containing 2-nitroimidazole compounds and methods of

making such reagents

INVENTOR (S):

Koch, Cameron J.; Lord, Edith M.

PATENT ASSIGNEE(S):

The Trustees of the Univ. of Pennsylvania, USA; The

University of Rochester

SOURCE:

U.S., 29 pp. Cont.-in-part of U.S. Ser. No.

978,918, abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5540908	Α	19960730	US 1994-286065	19940804
CA 2149770	AA	19940526	CA 1993-2149770	19931118
US 5843404	A	19981201	US 1996-598752	19960208
PRIORITY APPLN. INFO	·.:		US 1992-978918	19921119
			US 1994-286065	19940804

## OTHER SOURCE(S): MARPAT 125:162343

Novel nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compd. and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., protein conjugates of the compds., reductive byproducts of the compds., and adducts formed between the compds. and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistol. techniques, noninvasive nuclear medicine methods (PET, SPECT), or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

## 180208-73-5P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

180208-73-5 CAPLUS RN

1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoropropyl)- (9CI) (CA CN INDEX NAME)

## IT 152721-37-4P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hypoxia detection with 2-nitroimidazole compds. and

immunogenic conjugates)

RN 152721-37-4 CAPLUS

1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1994:506516 CAPLUS

DOCUMENT NUMBER:

121:106516

TITLE:

CN

Monoclonal antibody to nitroaromatic compound for

hypoxia detection

INVENTOR(S):

Koch, Cameron J.; Lord, Edith M.

PATENT ASSIGNEE(S):

University of Pennsylvania, USA; University of

Rochester

SOURCE:

PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND DATE		APPLICATION NO.	DATE
WO 9411348 W: CA, JP,	A1 199405	26	WO 1993-US11190	19931118
RW: AT, BE,	CH, DE, DK, E		GB, GR, IE, IT, LU	
CA 2149770 EP 669913	AA 199405 A1 199509		CA 1993-2149770 EP 1994-902291	
R: BE, CH, JP 08503469	DE, DK, FR, G T2 199604		LI JP 1993-512489	19931118
PRIORITY APPLN. INFO		10	US 1992-978918	19921119
			WO 1993-US11190	19931118

OTHER SOURCE(S): MARPAT 121:106516

AB Novel nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compd. and a carrier **protein** are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., the compds.' **protein** conjugates, the compds.' reductive byproducts, and adducts formed between the compds. and mammalian hypoxic cell tissue **proteins**. The invention is further directed to methods for detecting tissue **hypoxia** using immunohistol. techniques, non-invasive nuclear medicinal methods, or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

IT 152721-37-4DP, conjugates with albumin or lysozyme or Bowman-Birk
inhibitor

RL: PREP (Preparation)

(prepn. of, as immunogen, for raising monoclonal antibody, for hypoxia detn.)

RN 152721-37-4 CAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

IT 152721-37-4P

RL: PREP (Preparation)

(prepn. of, for prepg. immunogen for raising monoclonal antibody for hypoxia detn.)

RN 152721-37-4 CAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:101090 CAPLUS

DOCUMENT NUMBER: 120:101090

TITLE: Detection of hypoxic cells by monoclonal antibody

recognizing 2-nitroimidazole adducts

AUTHOR(S): Lord, Edith M.; Harwell, Lee; Koch, Cameron J.

CORPORATE SOURCE: Cancer Cent., Univ. Rochester, Rochester, NY, 14642,

USA

SOURCE: Cancer Res. (1993), 53(23), 5721-6

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal LANGUAGE: English

AB A pentafluorinated deriv. [EF5; 2-(2-nitro-1H-imidazol-1-yl)-N-(2,2,3,3,3-

pentafluoropropyl)acetamide] of etanidazole was synthesized with the expectation of lessening some of the non-oxygen-dependent variability in adduct formation obsd. previously with other nitroarom. compds. protein conjugates, prepd. by radiochem. redn., were found to be immunogenic and allowed the development of monoclonal antibodies. these antibodies, ELK2-4, has been characterized and found to be highly specific for the EF5 adducts whether produced radiochem. or by cellular bioreductive metab. The 9L rat glioma cells pretreated with EF5 under hypoxic, compared with aerobic, conditions were readily discriminated immunochem. using fluorochrome-conjugated secondary antibodies which recognize the ELK2-4 antibody subtype (IgG1). Similarly, the central region of multicellular spheroids, composed of EMT6 mouse mammary sarcoma cells, was selectively visualized by immunohistochem. after the spheroids were incubated for 4  $\bar{h}$  in 0.5 mM EF5. Tumor biopsy, prepn., and immunohistochem. staining 24 h after treatment of tumor-bearing animals with drug also demonstrated high contrast regions within EMT6 mouse or Morris 7777 hepatoma rat tumors. The use of this new compd. and its highly specific monoclonal antibody may allow elucidation of bioreductive metab. of the nitroheterocyclics and significantly improve technologies for the quantitation of tissue pO2.

IT 152721-37-4

RL: ANST (Analytical study)

(in hypoxic cell detection with monoclonal antibodies)

RN 152721-37-4 CAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI)

=> fil uspatful

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 6 Feb 2001 (20010206/PD) FILE LAST UPDATED: 6 Feb 2001 (20010206/ED) HIGHEST PATENT NUMBER: US6185737 CA INDEXING IS CURRENT THROUGH 6 Feb 2001 (20010206/UPCA) ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 6 Feb 2001 (20010206/PD) REVISED CLASS FIELDS (/NCL) LAST RELOADED: Nov 2000 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Sep 2000

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 full

11 L3

=> d 18 1-11 ibib abs hitstr

ANSWER 1 OF 11 USPATFULL

ACCESSION NUMBER: 1999:166572 USPATFULL

TITLE: INVENTOR(S): Metal chelating compounds having an SNNN donor set

Archer, Colin Mill, Chesham, United Kingdom Bower, Gary Robert, Aylesbury, United Kingdom Gill, Harjit Kaur, Chesham, United Kingdom Riley, Anthony Leonard Mark, Marlow, United Kingdom Storey, Anthony Eamon, Amersham, United Kingdom Canning, Lewis Reuben, Chesham, United Kingdom Griffiths, David Vaughan, Colchester, United Kingdom

PATENT ASSIGNEE(S):

Nycomed Amersham plc, United Kingdom (non-U.S.

corporation)

NUMBER DATE \_\_\_\_\_

PATENT INFORMATION: APPLICATION INFO.:

US 6004531 19991221 US 1997-917476 19970826 (8)

RELATED APPLN. INFO.:

Division of Ser. No. US 1997-888398, filed on 7 Jul 1997 which is a continuation of Ser. No. US 356383

NUMBER DATE -----

PRIORITY INFORMATION:

EP 1993-302634 19930402

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Clardy, S. Mark

ASSISTANT EXAMINER:

Hartley, Michael G. LEGAL REPRESENTATIVE: Wenderoth, Lind & Ponack, L.L.P.

NUMBER OF CLAIMS:

9

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

10 Drawing Figure(s); 10 Drawing Page(s)

LINE COUNT: 1544

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Ligands for radiopharmaceutical use are capable of chelating radiometal species and of being bound to biological targeting molecules. The ligands have formula (a) and (b), where A, A'=--SZ or Y, B.dbd.O or S, Y.dbd. (c), Z.dbd.H or a thiol protecting group, m=2 or 3, n=2 or 3,

 $\alpha = 0$ 

or 1, R.dbd.H or unsubstituted or substituted hydrocarbon and pharmaceutically acceptable salts, provided that at least one CR.sub.2 group represents CO and forms, together with an adjacent N atom, a --CONR-- amide group. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 164213-58-5P

(prepn. of metal chelating compds.)

164213-58-5 USPATFULL

CN 1H-Imidazole-1-acetamide,

N-[5-[[[(acetylamino)methyl]thio]acetyl]amino]-

6-[[2-(dimethylamino)ethyl]amino]-6-oxohexyl]-2-nitro- (9CI) (CA INDEX NAME)

ANSWER 2 OF 11 USPATFULL

ACCESSION NUMBER:

TITLE:

1999:89283 USPATFULL

INVENTOR(S):

Thioether-containing metal chelating compounds Archer, Colin Mill, Chesham, United Kingdom Bower, Gary Robert, Aylesbury, United Kingdom Gill, Harjit Kaur, Chesham, United Kingdom

Riley, Anthony Leonard Mark, Marlow, United Kingdom Storey, Anthony Eamon, Amersham, United Kingdom

Canning, Lewis Reuben, Chesham, United Kingdom

Griffiths, David Vaughan, Colchester, United Kingdom Nycomed Amersham plc, United Kingdom (non-U.S.

corporation)

NUMBER DATE

-----PATENT INFORMATION: US 5932707 19990803 APPLICATION INFO.: US 1997-888398 19970707

RELATED APPLN. INFO.: Continuation of Ser. No. US 356383

> NUMBER DATE

PRIORITY INFORMATION: EP 1993-302634 19930402 DOCUMENT TYPE:

Utility PRIMARY EXAMINER: Dees, Jose G. ASSISTANT EXAMINER:

Hartley, Michael G. LEGAL REPRESENTATIVE:

Wenderoth, Lind & Ponack, L.L.P. NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 10 Drawing Figure(s); 10 Drawing Page(s)

LINE COUNT: 1559

PATENT ASSIGNEE(S):

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Ligands for radiopharmaceutical use are capable of chelating radiometal species and of being bound to biological targeting molecules. The ligands have the formula (a) and (b), where A, A'=--SZ or Y, B=O or S, Y=(c), Z=H or a thiol protecting group, m=2 or 3, n=2 or 3, q=0 or 1, R=H or unsubstituted or substituted hydrocarbon and pharmaceutically acceptable salts, provided that at least one CR.sub.2 group represents CO and forms, together with an adjacent N atom; a --CONR-- amide group. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 164213-58-5P

(prepn. of metal chelating compds.)

164213-58-5 USPATFULL RN CN 1H-Imidazole-1-acetamide,

N-[5-[[[[(acetylamino)methyl]thio]acetyl]amino]-

6-[[2-(dimethylamino)ethyl]amino]-6-oxohexyl]-2-nitro- (9CI) (CA INDEX

ANSWER 3 OF 11 USPATFULL

ACCESSION NUMBER: 1998:150428 USPATFULL TITLE: Detection of hypoxia INVENTOR(S):

Koch, Cameron J., Phila., PA, United States Lord, Edith M., Rochester, NY, United States PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania,

Philadelphia, PA, United States (U.S. corporation) Trustees of the University of Rochester, Rochester,

NY,

United States (U.S. corporation)

NUMBER DATE PATENT INFORMATION:

US 5843404

19981201

APPLICATION INFO.:

US 1996-598752 19960208

RELATED APPLN. INFO.:

Division of Ser. No. US 1994-286065, filed on 4 Aug 1994, now patented, Pat. No. US 5540908 which is a continuation-in-part of Ser. No. US 1992-978918, filed

(8)

on 19 Nov 1992, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Achutamurth, Ponnathamurthy

LEGAL REPRESENTATIVE:

Woodcock Washburn Kurtz Mackiewicz & Norris LLP

NUMBER OF CLAIMS:

15

EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 1,9
18 Drawing Figure(s); 15 Drawing Page(s)

LINE COUNT:

1430

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

Novel nitroaromatic compounds and immunogenic conjugates comprising a novel nitroaromatic compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for

the

claimed nitroaromatic compounds, the compounds' protein conjugates, the compounds' reductive byproducts, and adducts formed between the compounds and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistological techniques, non-invasive nuclear medicinal methods, or nuclear magnetic resonance. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 152721-37-4DP, conjugates with albumin or lysozyme or Bowman-Birk
inhibitor

(prepn. of, as immunogen, for raising monoclonal antibody, for hypoxia  $\det n$ .)

RN 152721-37-4 USPATFULL

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

IT 152721-37-4P

(prepn. of, for prepg. immunogen for raising monoclonal antibody for hypoxia detn.)

RN 152721-37-4 USPATFULL

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

L8 ANSWER 4 OF 11 USPATFULL

ACCESSION NUMBER:

1998:42477 USPATFULL

TITLE:

Methods for preparing heteroatom-bearing ligands and

metal complexes thereof

INVENTOR(S):

Ramalingam, Kondareddiar, Dayton, NJ, United States Raju, Natarajan, Kendall Park, NJ, United States

PATENT ASSIGNEE(S):

Bracco International B.V., Amsterdam, United States

(non-U.S. corporation)

NUMBER DATE

PATENT INFORMATION:

US 5741912 19980421

APPLICATION INFO.:

US 1995-479076 19950606 (8)

RELATED APPLN. INFO.:

Division of Ser. No. US 1994-242093, filed on 18 May 1994, now patented, Pat. No. US 5608110 which is a continuation-in-part of Ser. No. US 1993-77981, filed

on 15 Jun 1993, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: ASSISTANT EXAMINER: Hollinden, Gary E. Hartley, Michael G.

LEGAL REPRESENTATIVE:

Hoare, George P.; Rhoads, Donald L.

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 6 1

LINE COUNT:

3388

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and

complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 161490-39-7P 161490-40-0P 161490-41-1P

(for prepn. of technetium triaza or oxadiaza dioxime complexes)

RN 161490-39-7 USPATFULL

CN lH-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)

RN 161490-40-0 USPATFULL

CN 5-Oxa-2,6,10-triazadodecanoic acid, 8-(hydroxyimino)-7,7-dimethyl-12-(2-nitro-1H-imidazol-1-yl)-11-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 161490-41-1 USPATFULL

CN 1H-Imidazole-1-acetamide,

N-[2-(hydroxyimino)-3-[[2-[[2-(hydroxyimino)-1,1-

dimethylpropyl]amino]ethoxy]amino]-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)

ANSWER 5 OF 11 USPATFULL

ACCESSION NUMBER:

1998:19731 USPATFULL

TITLE:

Fluorinated 2-nitroimidazole analogs for detecting

hypoxic tumor cells

INVENTOR (S):

Tracy, Michael, Palo Alto, CA, United States

Kelson, Andrew B., San Carlos, CA, United States

Workman, Paul, Wilmslow, England Lewis, Alexander D., Bearsden, Scotland Aboagye, Eric O., Bearsden, Scotland

PATENT ASSIGNEE(S):

SRI International, Menlo Park, CA, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION:

US 5721265 19980224

APPLICATION INFO.: RELATED APPLN. INFO.: US 1995-458178 19950602 (8)

Continuation-in-part of Ser. No. US 1994-286477, filed on 5 Aug 1994, now abandoned

Utility

DOCUMENT TYPE:

Higel, Floyd D.

PRIMARY EXAMINER: LEGAL REPRESENTATIVE:

Reed, Dianne E.Bozicevic & Reed LLP

47

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

1,38

NUMBER OF DRAWINGS:

10 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT:

1317

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Agents useful for detecting hypoxic tumor cells are provided. The compounds have the structural formula (I) ##STR1## Methods of using the compounds to detect hypoxic tumor cells are also provided, as are pharmaceutical compositions formulated with the novel compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

167648-73-9P 177595-17-4P 177595-20-9P 177595-21-0P 177595-22-1P 203452-63-5P

> (prepn. of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

RN 167648-73-9 USPATFULL

1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)-CN (9CI) (CA INDEX NAME)

177595-17-4 USPATFULL

CN 1H-Imidazole-1-acetamide,

N-(2-hydroxyethyl)-2-nitro-N-(3,3,3-trifluoro-2hydroxypropyl) - (9CI) (CA INDEX NAME)

RN 177595-20-9 USPATFULL

CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(hydroxymethyl)propyl]- (9CI) (CA INDEX NAME)

RN 177595-21-0 USPATFULL

CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(1-hydroxyethyl)propyl]- (9CI) (CA INDEX NAME)

RN 177595-22-1 USPATFULL CN 1H-Imidazole-1-acetamide, 2-nitro-N,N-bis(3,3,3-trifluoro-2-hydroxypropyl)-(9CI) (CA INDEX NAME)

RN 203452-63-5 USPATFULL

CN .beta.-D-Glucopyranoside, methyl 2-deoxy-2-[[(2-nitro-1H-imidazol-1-yl)acetyl](3,3,3-trifluoro-2-hydroxypropyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 6 OF 11 USPATFULL

ACCESSION NUMBER:

97:80883 USPATFULL

TITLE:

Heteroatom-bearing ligands and metal complexes thereof

INVENTOR (S):

Ramalingam, Kondareddiar, Dayton, NJ, United States

Raju, Natarajan, Kendall Park, NJ, United States Bracco International B.V., Amsterdam, United States

(non-U.S. corporation)

NUMBER DATE -----

PATENT INFORMATION:

PATENT ASSIGNEE(S):

US 5665329

19970909 19950606 (8)

APPLICATION INFO.:

US 1995-480048

RELATED APPLN. INFO.:

Division of Ser. No. US 1994-242093, filed on 18 May 1994 which is a continuation-in-part of Ser. No. US

1993-77981, filed on 15 Jun 1993, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Hollinden, Gary E.

ASSISTANT EXAMINER:

Hartley, Michael G.

LEGAL REPRESENTATIVE:

Hoare, George P.; Rhoads, Donald L.

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

LINE COUNT:

3429

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 161490-39-7P 161490-40-0P 161490-41-1P

(for prepn. of technetium triaza or oxadiaza dioxime complexes)

RN 161490-39-7 USPATFULL

CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2nitro- (9CI) (CA INDEX NAME)

161490-40-0 USPATFULL RN

CN 5-0xa-2,6,10-triazadodecanoic acid, 8-(hydroxyimino)-7,7-dimethyl-12-(2nitro-1H-imidazol-1-yl)-11-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

161490-41-1 USPATFULL RN

1H-Imidazole-1-acetamide,

N-[2-(hydroxyimino)-3-[[2-[[2-(hydroxyimino)-1,1dimethylpropyl]amino]ethoxy]amino]-3-methylbutyl]-2-nitro- (9CI) (CA

INDEX NAME)

ANSWER 7 OF 11 USPATFULL

ACCESSION NUMBER:

97:70702 USPATFULL

TITLE:

Polyaza heteroatom-bearing ligands and metal complexes

thereof for imaging or radiotherapy

INVENTOR(S):

Ramalingam, Kondareddiar, Dayton, NJ, United States

PATENT ASSIGNEE(S):

Raju, Natarajan, Kendall Park, NJ, United States Bracco International B.V., Amsterdam, United States

(non-U.S. corporation)

NUMBER DATE -----

PATENT INFORMATION:

US 5656254 19970812

APPLICATION INFO.:

RELATED APPLN. INFO.:

US 1995-471590 19950606 (8) Division of Ser. No. US 1994-242093, filed on 18 May 1994 which is a continuation-in-part of Ser. No. US

1993-77981, filed on 15 Jun 1993, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Hollinden, Gary E.

ASSISTANT EXAMINER: LEGAL REPRESENTATIVE: Hartley, Michael G. Hoare, George P.; Rhoads, Donald L.

NUMBER OF CLAIMS:

16

EXEMPLARY CLAIM:

LINE COUNT:

3551

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 161490-39-7P 161490-40-0P 161490-41-1P

(for prepn. of technetium triaza or oxadiaza dioxime complexes)

RN 161490-39-7 USPATFULL

1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-CN nitro- (9CI) (CA INDEX NAME)

161490-40-0 USPATFULL RN

5-0xa-2,6,10-triazadodecanoic acid, 8-(hydroxyimino)-7,7-dimethyl-12-(2-CN nitro-1H-imidazol-1-yl)-11-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

161490-41-1 USPATFULL RN

CN 1H-Imidazole-1-acetamide,

N-[2-(hydroxyimino)-3-[[2-[[2-(hydroxyimino)-1,1-

dimethylpropyl]amino]ethoxy]amino]-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)

ANSWER 8 OF 11 USPATFULL

ACCESSION NUMBER: 97:38628 USPATFULL

TITLE:

Heteroatom-bearing ligands and metal complexes thereof Ramalingam, Kondareddiar, Dayton, NJ, United States

INVENTOR(S): Raju, Natarajan, Kendall Park, NJ, United States

Bracco International B.V., Amsterdam, United States PATENT ASSIGNEE(S):

(non-U.S. corporation)

NUMBER DATE \_\_\_\_\_

PATENT INFORMATION: US 5627286 19970506 APPLICATION INFO.: US 1995-472058 19950606 (8)

Division of Ser. No. US 1994-242093, filed on 18 May RELATED APPLN. INFO.:

1994 which is a continuation-in-part of Ser. No. US

1993-77981, filed on 15 Jun 1993, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Hollinden, Gary E. Hartley, Michael G. ASSISTANT EXAMINER:

LEGAL REPRESENTATIVE: Hoare, George P.; Rhoads, Donald L.

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM: 1 LINE COUNT: 3404

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ΑB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

161490-39-7P 161490-40-0P 161490-41-1P IT

(for prepn. of technetium triaza or oxadiaza dioxime complexes)

RN 161490-39-7 USPATFULL

1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-CN nitro- (9CI) (CA INDEX NAME)

RN 161490-40-0 USPATFULL

CN 5-0xa-2,6,10-triazadodecanoic acid, 8-(hydroxyimino)-7,7-dimethyl-12-(2nitro-1H-imidazol-1-yl)-11-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

161490-41-1 USPATFULL RN

1H-Imidazole-1-acetamide, CN

N-[2-(hydroxyimino)-3-[[2-[[2-(hydroxyimino)-1,1dimethylpropyl]amino]ethoxy]amino]-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)

ANSWER 9 OF 11 USPATFULL  $r_8$ 

ACCESSION NUMBER: 97:18334 USPATFULL

TITLE:

Heteroatom-bearing ligands and metal complexes thereof INVENTOR(S): Ramalingam, Kondareddiar, Dayton, NJ, United States

Raju, Natarajan, Kendall Park, NJ, United States

PATENT ASSIGNEE(S):

Bracco International B.V., Amsterdam, United States

(non-U.S. corporation)

	NUMBER	DATE	
•			
PATENT INFORMATION:	US 5608110	19970304	
APPLICATION INFO.:	US 1994-242093	19940518 (8)	
RELATED APPLN. INFO.:	Continuation-in-	part of Ser. No.	US 1993-77981, filed

on 15 Jun 1993, now abandoned

Utility DOCUMENT TYPE:

Hollinden, Gary E. PRIMARY EXAMINER: Hartley, Michael G. ASSISTANT EXAMINER:

Hoare, George P.; Rhoads, Donald L. LEGAL REPRESENTATIVE:

6 NUMBER OF CLAIMS: 1 EXEMPLARY CLAIM:

3349 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Novel compounds containing a heteroatom-bearing bridge and novel AB complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 161490-39-7P 161490-40-0P 161490-41-1P 187847-72-9P

(prepn. of heteroatom-bearing bridged amine oxime ligands, analogs,

and

their metal complexes for use in diagnostic or therapeutic methods)

161490-39-7 USPATFULL RN

1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-CN nitro- (9CI) (CA INDEX NAME)

161490-40-0 USPATFULL RN

5-0xa-2,6,10-triazadodecanoic acid, 8-(hydroxyimino)-7,7-dimethyl-12-(2-CNnitro-1H-imidazol-1-yl)-11-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

161490-41-1 USPATFULL RN

1H-Imidazole-1-acetamide, CN

N-[2-(hydroxyimino)-3-[[2-[[2-(hydroxyimino)-1,1dimethylpropyl]amino]ethoxy]amino]-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)

187847-72-9 USPATFULL RN

L8 ANSWER 10 OF 11 USPATFULL

ACCESSION NUMBER:

96:67732 USPATFULL

TITLE:

Detection of hypoxia with reagents containing

2-nitroimidazole compounds and methods of making such

reagents

INVENTOR(S):

Koch, Cameron J., Philadelphia, PA, United States

Lord, Edith M., Rochester, NY, United States

PATENT ASSIGNEE(S):

The Trustees of the Univ. of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)

The University of Rochester, Rochester, NY, United

States (U.S. corporation)

NUMBER DATE

PATENT INFORMATION:

US 5540908 19960730 US 1994-286065 19940804

APPLICATION INFO.: RELATED APPLN. INFO.:

US 1994-286065 19940804 (8) Continuation-in-part of Ser. No. US 1992-978918, filed

on 19 Nov 1992, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Kim, Kay K. A.

LEGAL REPRESENTATIVE:

Woodcock Washburn Kurtz Mackiewicz & Norris

NUMBER OF CLAIMS:

31

EXEMPLARY CLAIM:

1
18 Drawing Figure(s); 15 Drawing Page(s)

NUMBER OF DRAWINGS: LINE COUNT:

1458

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel nitroaromatic compounds and immunogenic conjugates comprising a novel nitroaromatic compound and a carrier protein are disclosed. The

invention further presents monoclonal antibodies highly specific for

the

claimed nitroaromatic compounds, the compounds' protein conjugates, the compounds' reductive byproducts, and adducts formed between the compounds and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistological techniques, non-invasive nuclear medicinal methods,

immunohistological techniques, non-invasive nuclear medicinal methods, or nuclear magnetic resonance. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 180208-73-5P

(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

RN 180208-73-5 USPATFULL

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)

IT 152721-37-4P

(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

152721-37-4 USPATFULL RN

1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) CN (CA INDEX NAME)

$$\begin{array}{c|c} N & NO_2 \\ \hline & N & O \\ & \parallel \\ & CH_2-C-NH-CH_2-CF_2-CF_3 \end{array}$$

ANSWER 11 OF 11 USPATFULL

90:95206 USPATFULL ACCESSION NUMBER:

Fluorine-containing 2-nitroimidazole derivatives TITLE:

Kagiya, Tsutomu, Kyoto, Japan INVENTOR(S): Abe, Mitsuyuki, Kyoto, Japan

Nishimoto, Seiichi, Nara, Japan Shibamoto, Yuta, Kyoto, Japan Otomo, Susumu, Kounosu, Japan Tanami, Tohru, Tokyo, Japan

Shimokawa, Kazuhiro, Settsu, Japan Yoshizawa, Toru, Osaka, Japan Hisanaga, Yorisato, Ibaraki, Japan

Kyoto University of Honmachi, Kyoto, Japan (non-U.S. PATENT ASSIGNEE(S):

corporation)

Taisho Pharmaceutical Co., Ltd., Tokyo, Japan

(non-U.S.

corporation)

Daikin Industries, Ltd., Osaka, Japan (non-U.S.

corporation)

DATE NUMBER PATENT INFORMATION: US 4977273 19901211 US 1989-448909 19891212 (7) APPLICATION INFO.:

NUMBER DATE \_\_\_\_\_ 19881214 PRIORITY INFORMATION: JP 1988-315974

DOCUMENT TYPE: Utility Ford, John M. PRIMARY EXAMINER:

Whittenbaugh, Robert C. ASSISTANT EXAMINER:

Birch, Stewart, Kolasch & Birch LEGAL REPRESENTATIVE:

1 NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

1 Drawing Figure(s); 1 Drawing Page(s) NUMBER OF DRAWINGS:

609 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A 2-nitroimidazole derivative of the formula: ##STR1## wherein R.sub.f is a group of the following formula (II) or (III):

wherein X is a hydrogen atom or a halogen atom; R.sub.1 is a group of the formula: ##STR2## wherein R.sub.2 is a hydrogen atom, a hydroxyl group, a C.sub.1 -C.sub.3 alkyl group, a C.sub.2 -C.sub.4 acyl group, benzylidene or acetonide; R.sub.3 is a hydrogen atom or a C.sub.1 -C.sub.3 alkyl group; Z is a hydrogen atom, COOY, COOR.sub.3, CONHOY, CONR.sub.4 R.sub.5 (wherein R.sub.4 and R.sub.5 are hydroxyl group-containing C.sub.1 -C.sub.3 alkyl groups or hydrogen atoms; Y is

hydrogen atom or a monovalent metal atom), an amino group, a hydroxyl group or OR.sub.3; l is an integer of 1 to 3; o is an integer of 0 to 3; p is an integer of 0 to 2; q is an integer of 0 to 3; m and n are integers of 0 to 4; and 1.ltoreq.m+n.ltoreq.4 or ##STR3## wherein R.sub.3, X and p are the same as defined above; Z' is the same as Z or is OCOOCH.sub.3; r is an integer of 1 to 3; s is 0 or 1; t is an integer of 0 to 4 provided that when p=0, s.noteq.0 and at least one X is a fluorine atom; and a radiosensitizer comprising said

nitroimidazole derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 130777-35-4P

(prepn. of, as radiosensitizer)

RN 130777-35-4 USPATFULL

CN 1H-Imidazole-1-acetamide, N-(3-amino-2,2-difluoro-3-oxopropyl)-2-nitro-(9CI) (CA INDEX NAME)

=>

=> save hypoxia/l

ENTER L#, L# RANGE, ALL, OR (END):all

L# LIST L1-L8 HAS BEEN SAVED AS 'HYPOXIA/L'

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	55.22	224.55
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION